	Percentage of Moisture
Phytolacca:—	
The roots carefully cleaned by washing, and dried at about 80° Cent. One-year-old plants, average of 48 samples	74.9
Apocynum:—	
The roots and rhizomes carefully cleaned by washing, and dried at room temperature. Average of 6 samples	60.00

Department of Pharmacognosy, College of Pharmacy, University of Minnesota, Minneapolis.

A CRITICISM OF THE UNITED STATES PHARMACOPŒIAL DESCRIPTIONS OF VEGETABLE DRUGS.

A THESIS SUBMITTED TO THE FACULTY OF PURDUE UNIVERSITY.

CHALMERS JOSEPH ZUFALL.

INTRODUCTION.

The inspection of crude drugs in a pharmaceutical manufactory requires continual reference to the descriptions of official drugs in the United States Pharmacopœia. While these descriptions are considered authentic, the question often arises, are they really accurate and correct for commercial drugs? Comments and criticisms are repeatedly found in the pharmaceutical journals which lead one to suspect inaccuracy on the part of the pharmacopœia committee which wrote these, and the purpose of this investigation is to determine how well these descriptions can be applied to the drugs of commerce and to authentic specimens.

The drugs are to be taken, one at a time, and large quantities of the material studied. The conditions for this study at the Eli Lilly and Company's plant are almost ideal, for we are able to see more than a mere sample from each bag; we can see the entire contents of the bags and bales as they are emptied in the mill-room ready for grinding. Then the pharmacopœial description is compared with as many authentic specimens as possible. The herbarium specimen is first checked up with the botanic authorities and then the crude drug, the herbarium specimen and the pharmacopœial description are compared. In many cases, three to five mounted specimens of the one species from widely-separated regions were used, thus giving any variations due to climatic conditions.

Aconite:—The six lots and ten samples examined show that the pharmacopœial description is correct for Aconitum napellus except as to the thickness of the root. Many roots were found to be 35 mm. in diameter at the crown. The pharmacopœia gives this diameter as "10 to 20 mm." It should be given as "10 to 35 mm. in diameter at the crown."

In order to aid in distinguishing the official drug from A. fischerii, which is being offered on the market as the true aconite, the pharmacopœia should add that the "starch grains are 4 to 12 microns in diameter." Those of A. fischerii are much larger, being 10 to 22 microns.

Apocynum:—The pharmacopœial description of Apocynum is "The dried rhizome of Apocynum Cannabinum, *Linne*, or of closely allied species of Apocynum.

The phrase "or of closely allied species of Apocynum" should be omitted, for this includes A. androsaemifolium, a "closely allied" species, so closely resembling A. cannabinum that it is difficult to distinguish between the two species, even when the plants are in flower. Yet, A. androsaemifolium has different medicinal properties and is used under the name of "Bitter Root." The foremost pharmaceutical botanists admit that they do not know the difference, and Henry Kraemer of the Philadelphia College of Pharmacy states that the only difference between these two roots is the presence of stone cells in the cortex of A. androsaemifolium and not in A. cannabinum. We have collected several specimens of the different species of Apocynum and are trying to establish the differences between these two species.

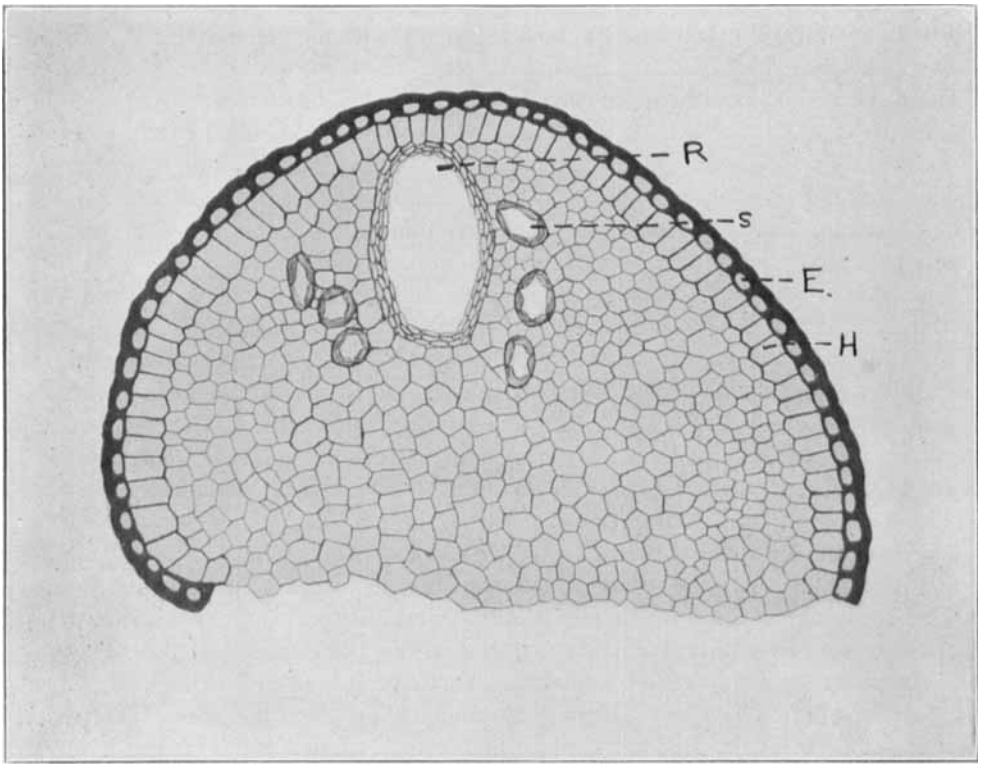

PLATE I.

SAVIN ADULTERANT—TRANSVERSE SECTION OF LEAF.

E, Epidermis; H, Hypodermis; R, Resin duct; S, Sclerotic cells.

Belladonna Leaves:—Belladonna leaves are often adulterated with the leaves and fruit of Scopola carniolica. The leaves of this adulterant resemble those of Belladonna so closely that it is almost impossible to detect it unless the fruit is present. So it seems wise to replace the phrase "frequently with the flowering tops intermixed," with the following, "usually with the tops possessing the dark brown or black, globular, indehiscent fruit, showing above the reflexed calyx.

lobes." This will exclude the tops of Scopola which usually possess the yellow or light brown, subglobular, transversely dehiscent fruit which is almost completely enclosed by the thin, paper-like calyx.

The requirement of 0.3% alkaloids is too low for Belladonna leaves. In 61 assays of samples and lots made in the last five years only three have been as low as 0.3%. The average of these 61 assays is 0.44%. This indicates that the pharmacopœial requirement is too low for prime drug and should be raised to at least 0.4%.

Berberis:—During the examination of six lots, many Berberis roots were found to be 40 mm. in diameter so that the size should be changed from "3 to 20 mm." to "3 to 40 mm."

A peculiarity of Berberis not seen in other roots is that it splits upon drying. It would be well to state this in the pharmacopœia as one of the characteristics of Berberis.

Buchu:—It is impracticable to obtain Buchu without some stems. Some of these stems are thick, woody and undoubtedly inert while "others are thin and contain the active constituent in considerable amount." (1)

The *per cent.* and character of these stems should be controlled by the pharmacopœia.

The stems in five lots and of seven good samples offered for sale average .8%. The pharmacopœia should exclude Buchu containing more than 10% stems. The stems permitted should not be more than 1 mm. in diameter.

Capsicum:—During the last year, it was found difficult to obtain the real Capsicum fastigiatum. The Japanese pepper was offered continually for Capsicum. The small Japanese variety answers the pharmacopœial description, but they are of a lower quality and are less pungent. The description should include the following and thereby exclude all but the genuine Capsicum. "The cells of the pericarp are usually quadrilateral, 20 to 55 microns in diameter, more or less wavy in outline, walls indistinctly beaded and, which is most noticeable, arranged in distinct longitudinal rows." (2)

Cardamom:—While the pharmacopœia describes the cardamom "fruit" as official, it adds that "the seeds alone contain active and valuable constituents."

The seeds alone should be made official, since they alone are of value, and thereby lessen the amount of inert material in the preparations.

These inert pods may vary considerably, for some pods may be full while others may contain only a few seeds or may be empty. These empty pods, being much lighter than the seeds, will accumulate at the tops of the bag on being handled. Thus the druggist may get a large *per cent.* of pods in his first preparations made from a bag, while there may be very few in the last preparations; thus his products will vary considerably.

Since the seeds or "decorticated cardamoms" are plentiful on the market, there seems no reason why they should not be made official instead of the "fruit."

Coca:—The requirement of "0.5% ether-soluble alkaloids" is too low.

The average of 21 assays of lots and samples is .85% ether-soluble alkaloids, the lowest assaying .66%.

From these results it seems that the requirement should be raised to at least .75% ether-soluble alkaloids, for, if Coca leaves are properly gathered, properly

shipped and properly stored, they will give a much higher assay than the pharmacopœia requires.

Colchicum Seed:—The pharmacopœia requires only 0.45% Colchicine which would include rather poor seed. The average of 18 assays is .66% colchicine, the lowest being .53%.

These results indicate that first-class Colchicum seed will assay at least 0.6% colchicine, and the pharmacopœial requirement should be raised to this *per cent.*

Cubeb:—Cubeb berries grow in spikes, and in gathering the drug the whole spike is picked, which includes the peduncle. In drying and handling the drug, the berries become detached from the peduncles, which then occur as "stems."

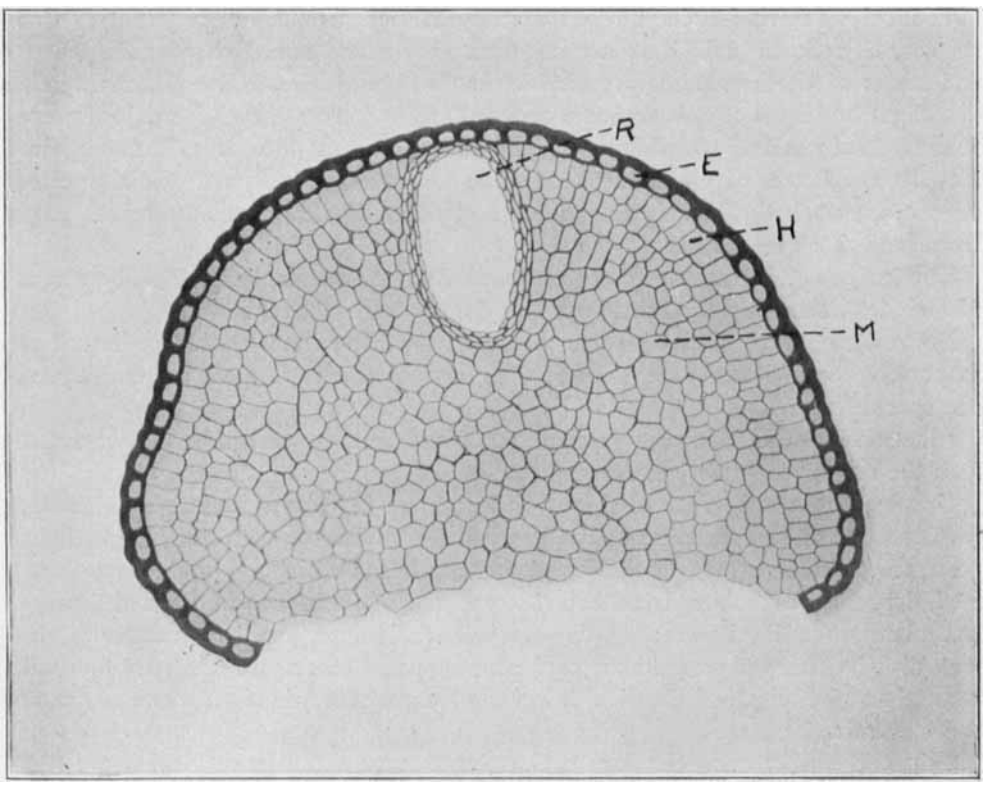

PLATE II.

JUNIPERUS SABINA—TRANSVERSE SECTION OF LEAF.

E, Epidermis; H, Hypodermis; R, Resin duct; M, Mesophyll.

Some berries on the market have no stems at all, while others have an excess of them. This indicates that the stems are removed from a part of the drug, for which a higher price is obtained, and these stems mixed with other lots and the average price obtained for it.

If stems are not deliberately added to Cubebs they will make a rather constant *per cent.* of the drug, so the pharmacopœia should specify that there shall not be more than 10 *per cent.* stems, and these should not be more than two mm. in diameter.

Ergot:—The examination of six lots, consisting of 154 bags, indicates that a few changes should be made regarding the color of the fracture and the pharmacopœia made to read as follows: "fracture short, gray, pinkish, blue or purple," instead of "pinkish, or reddish-white."

The thickness should be "from 3 to 5 mm." instead of "about 3 mm."

Grindelia:—The pharmacopœia states, "The dried leaves and flowering tops of Grindelia robusta and G. squarrosa," but does not state how much of the "tops." Since the activity of this drug evidently resides in the resinous exudation and since the resin is not found in the larger stems, the length of the "flowering tops" should be given so as to exclude the larger, inert stems. The maximum length should be 30 cm.

From the description in the pharmacopœia, one would infer that the two species, G. robusta and G. squarrosa, were very much alike, whereas the leaves and scales of the involucres are distinct in the two species. The pharmacopœia describes the leaves as "about 5 cm. or less long," whereas leaves 7 cm. long were found. "Lanceolate" should not be used in describing the leaves because that includes the leaves of G. Lanceolata, while the leaves of the two official species do not approach the lanceolate shape. Instead of "pale green" the leaves vary from pale green to greenish yellow.

The leaves are further described as "somewhat coriaceous, brittle." The leaves of Grindelia become very brittle upon drying and are not coriaceous.

From these discrepancies it seems best that the two species should be described separately because very often lots of drug arrive which are made up entirely of one species.

It seems that the following descriptions would be more scientific and workable than the one given in the pharmacopœia:—

Grindelia robusta:—Leaves 7 cm. or less long, broadly spatulate or obovate, sessile, more or less clasping at the base, finely to coarsely serrate, obtuse, light green to greenish-yellow, finely dotted, brittle; heads resinous-viscid, many-flowered, depressed-urceolate, 1 cm. broad, composed of numerous imbricated, linear-lanceolate spreading bracts; ray-flowers yellow, ligulate, pistillate sometimes absent, disk-flowers yellow, tubular, perfect; pappus of two or three mostly unequal awns about the length of the disk-flowers; taste pungent and bitter, odor aromatic and balsamic.

Grindelia squarrosa:—Similar to G. robusta except the leaves which are 4½ cm. or less in length and 8 to 15 mm. wide, usually decidedly oblong or oblong spatulate, obtuse, more or less clasping at the base, sharply spinulose-dentate, sometimes lacinite. The bracts of the involucre strongly squarrose.

Lupulin:—The results of examining five lots and 16 samples indicate that prime Lupulin has an amber-yellow color which should be given instead of "brownish-yellow." The latter color is seen only in drug which is not fresh.

There have been suggestions that the maximum ash limit is too low, but from our experience we know that it is not. Careless handling or willful adulteration are the only causes for the presence of the foreign mineral substance which causes the high ash in some Lupulin.

Savin:—The pharmacopœial description of Sabina is not specific enough to exclude several other species of Juniperus. Consequently, these other species are

found on the market offered for savin. The oils of these species are inactive and undoubtedly this is the cause of savin falling into disuse.

It is difficult to identify a species of the Juniperus from a twig alone, without specimens of the fruit and without knowledge of the form and habit of growth of the plant. The difficulty is twofold. In the first place, two plants which undoubtedly belong to one species, develop, if grown under varying conditions of soil and climate, very marked differences, both in general habit and in the character and mode of arrangement of the leaves. Juniperus sabina when found in the natural state, has decussate, ovate-lanceolate leaves, while the cultivated plant bears leaves which are more needle-like and sometimes in whorls of threes.

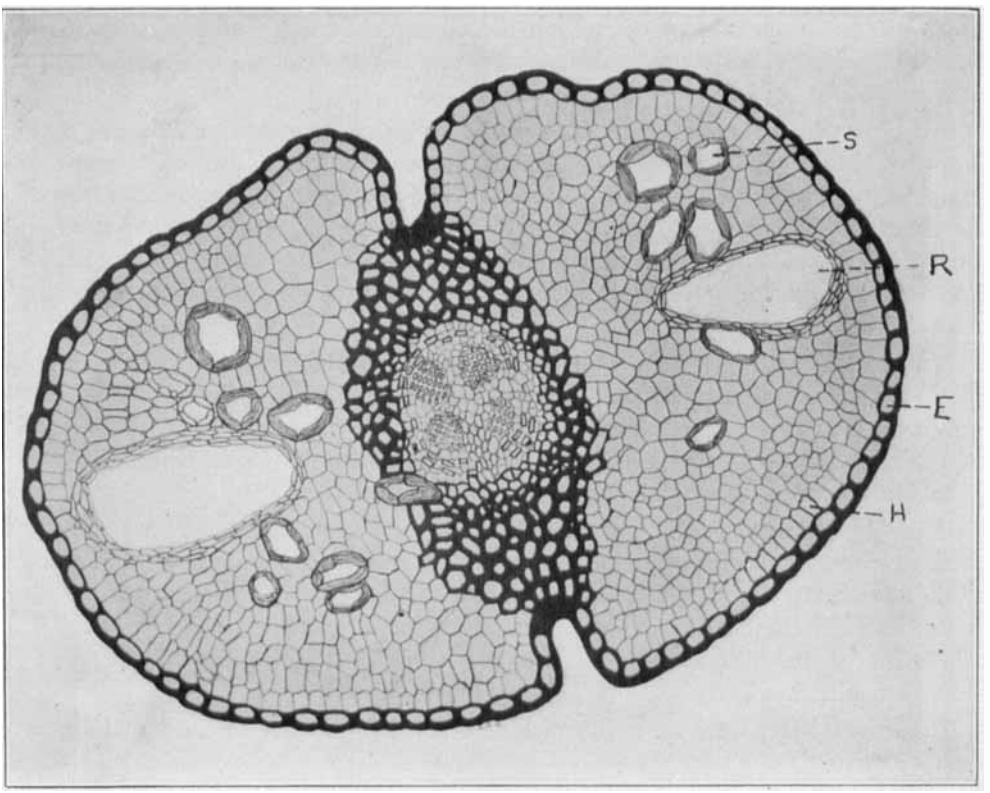

PLATE III.

JUNIPERUS OCCIDENTALIS—TRANSVERSE SECTION OF TWIG AND TWO LEAVES.
E, Epidermis; H, Hypodermis; R, Resin duct; S, Sclerotic cells.

In the second place, plants of different species have adopted a similar habit; for instance, forms of J. sabina, J. phœnicea, J. thurifera, J. barbadensis, J. virginiana, L. and J. scopulorum, Sarg. possess closely imbricated, acute or acuminate leaves, tightly appressed to the stems, and are externally almost indistinguishable one from another.

So variable are some of these plants that, of J. Sabina, seven varieties are recognized by Biessner and described by him in his "Handbuch der Nadelholzkunde."

In 1902, there was published by the Ecole Superieure de Pharmacie, Paris, a

thesis by H. Henri Mongin, entitled "Etude Anatomique de la fenille des Juniperinees." He pointed out that, in the drug of commerce, besides J. sabina, there were to be met with J. thurifera, L., and its variety gallica, and J. phœnicea, L. Most people would find it practically impossible to distinguish non-fruiting twigs of these species from the typical form of J. sabina. All have small leaves, closely appressed to the stem, giving the branches a cylindrical appearance. With fruiting specimens available, J. phœnicea is readily separated, having larger yellowish fruits, while the fruits of J. sabina and J. thurifera are small and bluish, resembling those of J. communis.

In 1874, M. E. Collin pointed out that the leafy twigs of J. phœnicea substituted for those of savin in French commerce. In 1902, M. Mongin found that they were still so employed in France, and indeed constituted the greater part of the drug met with in that country. He also points out that the oil of J. phœnicea is inactive, being similar to that of J. communis.

Mongin's work renders it possible to distinguish between J. sabina and these substitutes, even when only the young branchlets, usually met with in the commercial drug, are available for examination. J. sabina and J. thurifera and its varieties have the leaves in pairs, each pair being at right angles to the succeeding pair, i. e., they are decussate. In J. phœnicea, on the other hand, the leaves are not decussate, but are arranged more or less spirally with five leaves inserted almost at the same level.

Mongin further shows that large sclerotic or stone cells are found in the mesophyll of the leaf of J. phœnicea and less abundantly in J. thurifera, whilst they are completely absent in J. sabina. Another point of difference is the continuance of the hypodermal layer over the resin duct in the leaf of J. phœnicea, while in J. sabina the resin duct abuts directly on to the epidermis.

In 1905, Freeman stated that there occurred in commerce in Great Britain a form of savin "with more convex, less acute leaves, which are so closely appressed to the stem as to give a cylindrical appearance to the branchlets, very different it is true from the typical savin, but so closely resembling some of the forms of J. sabina that in the absence of fruit it is impossible to separate them by a microscopic examination." (3).

From these references we may conclude that savin has been adulterated for at least 40 years.

For some time there have been large quantities of so-called savin on the market which consists of twigs resembling somewhat the twigs of J. sabina, but the leaves are more convex, less acute and have an oval gland. By careful inspection it is noted that the arrangement of the leaves is not the same on all twigs. The drug is a mixture of about one-half twigs whose leaves are in whorls of threes and one-half twigs having decussate leaves. Branching twigs showed a peculiarity in that the branch had decussate leaves while the leaves of the twig were in whorls of threes. The latter fact indicates that the pharmacopœia is at fault, for these branchlets answer its requirements while the main twig of the same species does not.

In microscopic sections of this substitute, both the decussate leaves and those in whorls of threes, show the following characteristics as brought out in plate 1;

large sclerotic or stone cells in the mesophyll beside the resin ducts and the hypodermal layer extending between the resin duct and the epidermis.

A pressed herbarium specimen of J. Sabina showed the leaves all decussate, apex decidedly acute, longer, less convex and the gland linear-oblong. Microscopic sections show the absence of sclerotic of stone cells and the resin duct abuts directly on to the epidermis as shown in plate II. These characteristics indicate that, according to M. Mongin, the pressed specimen is properly named and that this substitute is not obtained from J. sabina. The leaves of the commercial drug are not arranged spirally, hence it is not obtained from J. phœnicea and the

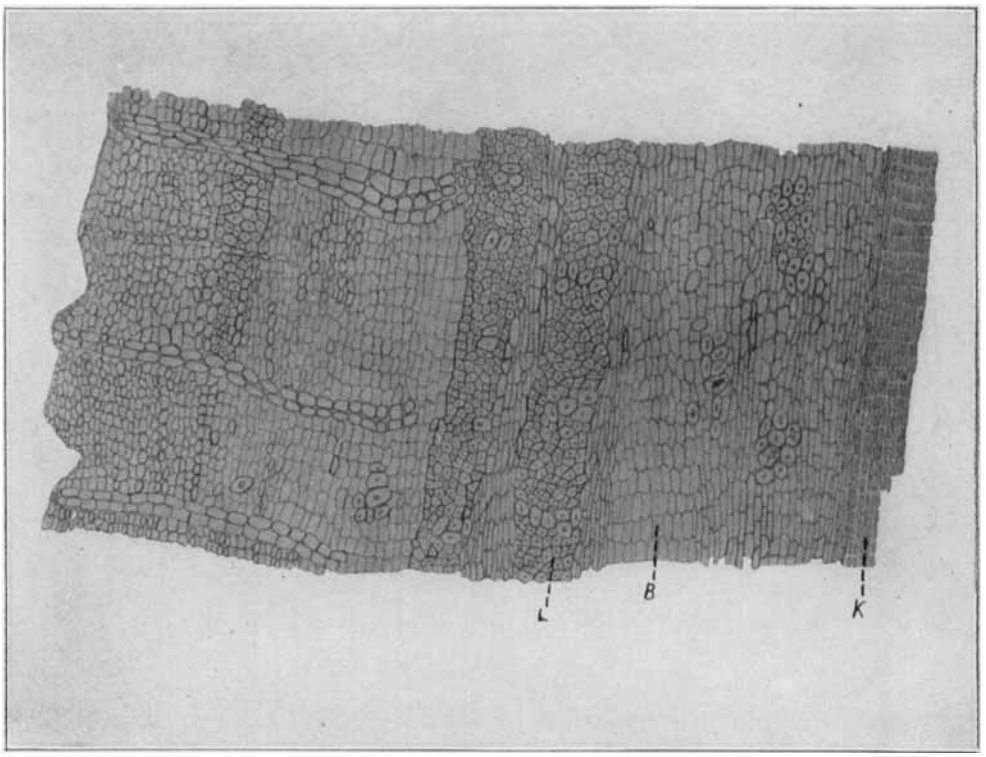

PLATE IV.

CRAMP BARK—COMMERCIAL DRUG—TRANSVERSE SECTION OF BARK.

B, Bark; L, Bast; K, Corky layer.

leaves are not all decussate, hence it is not J. thurifera. But pressed specimens of J. occidentalis, Hook, have short, oval, convex leaves with stone cells beside the resin duct and the resin duct separated from the epidermis by the hypodermis. This form shows the peculiarity of having the leaves in whorls of threes on the large branches, but the branchlets from these have decussate leaves. This indicates that the substitute which has been offered for savin is undoubtedly from J. occidentalis.

Three specimens of J. sabina obtained from the New York Botanic Garden show the following characteristics in contrast with those of this substitute; leaves

spreading, acuminate, all decussate no stone cells in the mesophyll and the resin duct abutting directly on to the epidermis."

In order to exclude all but J. sabina the pharmacopœial description should read as follows:—

Thin quadrangular branches bearing green, decussate leaves which are scale-like, ovate-lanceolate, acute or acuminate, appressed or spreading, imbricated; having on the back a shallow groove containing a linear-oblong gland; odor strong, penetrating, terebinthinate; taste disagreeable, resinous and bitter. In cross-section the leaves should show no stone cells and the resin duct abutting directly on to the epidermis."

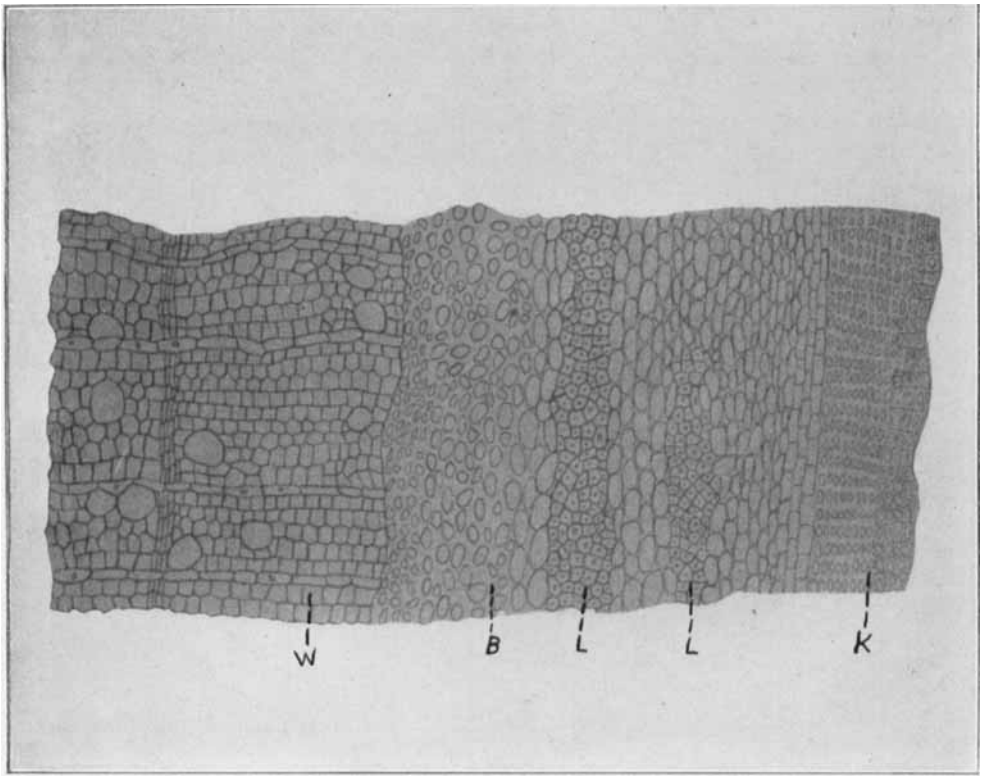

PLATE V.

ACER SPICATUM—TRASVERSE SECTION OF BARK AND WOOD.

B, Bark; L, Bast; K, Corky layer; W, Wood.

The fact that the pharmacopœia states that the leaves are dark green and have an oblong or roundish gland indicates that the description may have been made from commercial drug and not from known specimens of J. sabina.

Scoparius:—A more definite description would be obtained if, "Thin, flexible branched twigs, 2 to 3 mm. thick, externally dark green" were replaced by "Flexible, round light-green branches with five low, narrow ridges, 2 to 3 mm. thick; the smallest branches being uniformly 1 to 15 mm. thick, dark green, with five distinct wings."

Viburnum Opulus:—The pharmacopœia states, "The dried bark of Viburnum opulus *Linne*," and then describes the bark of Acer spicatum. Consequently the Cramp Bark on the market for the last twenty years has been the bark of Acer spicatum and, although it answers the pharmacopœial description, it is not the bark desired.

In 1912, Nathan S. Slatter, of Bennington, Vt., discovered that the Cramp Bark on the market was not the same as the bark of Viburnum opulus, but was that of Acer spicatum. He exposed the fact to Oliver A. Farwell, of Detroit, who confirmed Slatter's statement by comparing Cramp Bark of commerce with authentic specimens of Viburnum opulus and Acer spicatum.

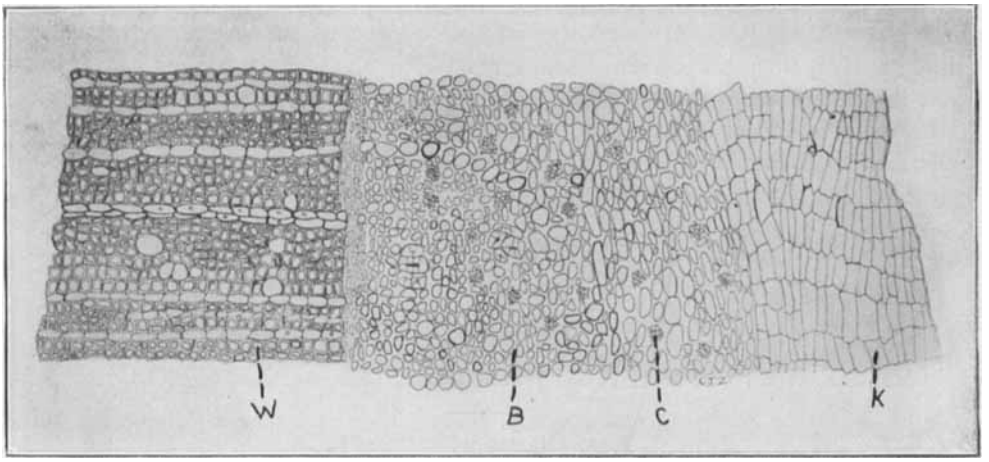

PLATE VI.

VIBURNUM OPULUS—TRANSVERSE SECTION OF BARK AND WOOD.

B, Bark; W, Wood; C, Calcium oxalate crystals; K, Corky layer.

1. H. H. Rusby in Merck's Report, Vol. XIX, p. 134.
2. Winton "Microscopy of Vegetable Foods," pp. 523 and 524.
3. "A Comparison of The Savin Leaves of Commerce," by Wm. G. Freeman in The Pharmaceutical Journal for Dec. 16, 1905, p. 829.
4. "Confusion Over Cramp Bark," by Oliver A. Farwell. The Bulletin of Pharmacy, Vol. 27, p. 65.

"Manual of the Trees of North America," by Charles Sprague Sargent.
"New Manual of Rocky Mountain Botany," Coulter and Nelson.
"Illustrated Flora of the Northern States and Canada," Britton and Brown.
"Flora of The Southeastern United States," John K. Small.
"Pflanzenfamilien," Engler and Prantl.
British Pharmaceutical Codex.

Farwell found that in 1895, a pharmacopœial committee of revision which tried to show the difference between Viburnum opulus and Viburnum prunifolium, used Acer spicatum for an authentic specimen of Viburnum opulus. This specimen was obtained from a large pharmaceutical manufactory and indicates that A. spicatum was used at that time for Cramp Bark. (4)

The sixth revision of the pharmacopœia under Viburnum opulus gives characistics undoubtely those of Acer spicatum. Such characteristics as "fracture tough, the tissues separating in layers," are surely not those of V. opulus, for the bark of the latter is very brittle and gives a sharp, clean fracture.

The findings of these two men led F. A. Miller to investigate the situation. He

obtained specimens of both Acer spicatum and Viburnum opulus from Arnold Aboretum, Missouri Botanic Garden, Baltimore Nursery, Kew Botanic Garden, and the German Botanic Garden. Sections and drawings of these were made and of commercial Cramp Bark. See plates 4 and 5. These drawings show clearly that commercial Cramp Bark is taken from Acer spicatum, for both show the bands of bast fibres and the absence of calcium oxalate.

The accompanying illustrations are representative of all the drawings made and show the desired points.

The pharmacopœia should replace the present description by the following:—"In transversely curved pieces or quills, of variable length, and one mm. or less thick; outer surface gray, longitudinally furrowed, small oval lenticels; inner surface brownish yellow, very smooth; fracture short and clean; transverse sections show an abundance of calcium oxalate crystals in rosettes, no bast fibres; taste at first bitter and then astringent."

Viburnum Prunifolium:—Two characteristics of this drug should be added which will aid considerably in its identification. These are the sour odor and the peculiar, short, smooth striæ on the inner surface of the bark.

Laboratories of Eli Lilly & Company, June, 1914.

REVIEW OF CURRENT PHARMACEUTICAL LITERATURE.*

PROF. JULIUS W. STURMER.

PHARMACEUTICAL ERA. (January.)

Stable Bichloride Solution:—Mercuric Chloride in aqueous solution containing also Sod. Silicate Sol. does not precipitate with ammonia. As the resulting ammoniacal sol. does not attack steel instruments, it may be found serviceable by the surgeon.

NOTE.—The author does not give bactericidal power of this solution as compared with ordinary Bichloride Sol. (J. W. S.)

Saccharin (and in particular its sodium salt) is converted into a bitter compound by action of fruit acids. The change takes place slowly at ordinary temperatures, more rapidly on application of heat.

CHEMICAL ABSTRACTS. (Jan. 20.)

Temperature of slaking lime:—1. At temperatures of about 270-300° wood is partially carbonized, and in the presence of oxygen, i.e., air, it ignites. A sample of lime from marble was found to attain a temperature of 390° during slaking, and the experiment proved that the slaking lime could ignite wood.

PHARMACEUTICAL JOURNAL. (Jan. 2.)

Ammoniated Mercury, constitution of:—The reaction with Hydrofluoric acid:— $2NH_2 Hg Cl + 4HFl = Hg Cl_2 + Hg Fl_2 + 2NH_4Fl$ points to the formula $Hg Cl NH_2$. That is, Mercuric Chloride with one Chlorine atom replaced by NH_2.

JOURNAL OF INDUSTRIAL AND ENG. CHEMISTRY. (February.)

Hard Wood Distillation Industry in America:—Interesting nine-page article by Edward H. French and James R. Withrow.

---

*Read before Philadelphia Branch, February meeting.